Original Study

# Characteristics and Clinical Outcomes of Sarcomatoid Carcinoma of the Lung

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## Abstract

**Sarcomatoid carcinoma is a rare subtype of lung cancer. We analyzed the clinicopathologic data from 93 patients treated at 2 institutions. The median survival was 16.4 months for the patients who underwent surgery and 4.3 months for those with metastases. The response to first-line chemotherapy was low, and a platinum-based combination was the more efficient option. New therapeutic strategies are needed for this disease.**

**Background:** Sarcomatoid carcinoma is a rare subtype of non–small-cell lung cancer, which has aggressive behavior. We present information on the clinicopathologic characteristics and clinical outcomes of these tumors. **Patients and Methods:** From January 2000 to December 2012, the clinicopathologic data from 93 patients treated at 2 French cancer centers were retrospectively analyzed. A pathologic review was performed of all tumors. **Results:** The patients were commonly male (77%), with a median age of 63 years and a history of smoking (84%). Most had symptoms, and about 70% presented with locally advanced or metastatic disease at diagnosis. Of the 93 cases, 41 were diagnosed by surgical resection. Pleomorphic carcinoma was the most common subtype (64%). With a median follow-up period of 30.7 months, the median survival of the patients who had undergone surgery was 16.4 months. Recurrence with distant metastases was common. Univariate analyses showed that advanced disease (pathologic stage > III) conferred a worse prognosis for recurrence-free and overall survival ($P = .0024$ and $P < .0001$, respectively). Twenty-eight patients received first-line chemotherapy for advanced disease. The progression rate was 72% at the first evaluation. The median time to progression and the median overall survival were poor (2.7 and 4.3 months, respectively). On univariate analysis, a platinum-based combination had significant influence on overall survival compared with monotherapy ($P < .0001$). **Conclusion:** Sarcomatoid carcinoma is associated with a poor prognosis. Surgical treatment should be carefully considered in the early stages. The high resistance to chemotherapy emphasizes the need to test for new strategies through collaborative programs dedicated to this population.

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## Introduction

Sarcomatoid carcinoma (SC) of the lung is a rare, poorly differentiated, subtype of non–small-cell lung carcinoma (NSCLC) and constitutes approximately 0.1% to 0.4% of all lung cancer cases.[1,2] The revised 2004 World Health Organisation (WHO) classification identified 5 subgroups: pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, carcinosarcoma, and pulmonary blastoma.[1] SC has been reported to be associated with a poor prognosis

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compared with other NSCLC subtypes. In the Surveillance, Epidemiology, Endpoints, and Results database, the SC histologic type was associated with a significantly poorer outcome at an early stage of NSCLC.[2]

The main caveats of the published data have been the limited size of the series owing to the rarity of the disease, the frequent mix of SC with poorly differentiated NSCLC owing to the difficulty of the pathologic diagnosis, and the lack of long-term follow-up data. In the present study, we analyzed a large 2-center series of patients with a strictly confirmed diagnosis of SC. We analyzed the clinicopathologic characteristics, prognostic factors, and clinical outcomes of a large series of 93 patients with SC of the lung to better understand and treat this subset of patients.

## Patients and Methods

### *Patients and Pathologic Studies*

The present study included a consecutive series of identified patients with SC of the lung. All patients pathologically proven to have SC were included, regardless of the disease stage. The patient data were screened from the archival records from January 2000 to December 2012 and collected at 2 French medical centers (Centre Hospitalier Universitaire de Toulouse and Institut René Gauducheau, Nantes). The data were anonymized and then analyzed in Toulouse, France.

The pathologic diagnoses had been made after surgical resection, endobronchial or transbronchial biopsy, or an autopsy. All specimens were reviewed centrally by a lung cancer pathologist and were classified according to the revised 2004 WHO classification of lung tumors.[1] Tumors containing epithelial components and $\geq$ 10% of a sarcomatoid component (spindle cell or giant cell, or both) were classified as pleomorphic carcinoma. Carcinosarcoma contains a mixture of carcinoma and a sarcomatous component (eg, chondrosarcoma, osteosarcoma, or rhabdomyosarcoma). Spindle cell carcinoma and giant cell carcinoma will be entirely composed of spindle or giant cells, respectively. Pulmonary blastoma is a very rare type of SC characterized as a biphasic tumor containing a primitive epithelial component resembling a well-differentiated fetal-type adenocarcinoma and a primary mesenchymal stromal component.

Biopsy specimens that contained sarcomatoid elements were not classified according to the 2004 WHO classification but were included as "nonspecific SC" because of the difficulty in finding a mixture of the 2 components in small tumor samples. After reviewing the data, 5 cases were ruled out by the pathologists. A total of 93 confirmed cases of SC were retained for our study.

### *Clinical Data*

All available clinical data were obtained from the clinical records and reports from the referring physicians. Electronic mail and/or letters were sent to contributors for additional information. At the diagnosis, baseline clinical data had been collected. The preoperative radiologic data, histologic features, adjuvant and neoadjuvant management, surgical procedures, and data on recurrence and survival in the early stages were also recorded. The medical and radiotherapy procedures, overall response to treatment, and data on survival in advanced and metastatic stages were reviewed retrospectively. The endpoint was defined as March 1, 2013.

All tumors were staged using the 7th edition of the TNM staging system of lung cancer.[3] The computed tomography (CT) scans were retrospectively analyzed. The responses were defined as the best response from the start of treatment until disease progression, according to the Response Evaluation Criteria In Solid Tumors, version 1.1, guidelines.[4] Relapse-free survival was defined as the interval between the diagnosis and relapse. The time to progression was defined as the interval from the start of treatment until disease progression. Overall survival was defined as the interval from the start of treatment until death from any cause.

### *Ethical Considerations*

All the patients, except for the 2 diagnosed by autopsy, provided written informed consent to their physicians according to the local regulations for observational studies for the collection of anonymized clinical and biologic data. The institutional review board from the University Hospital of Toulouse (France) approved the study for central data analyses. The patient data were anonymized and forwarded to the central statistical office in electronic format.

### *Statistical Analysis*

The data were summarized by frequency and percentage for categorical variables and by the median and range for continuous variables. Comparisons between groups were performed using the $\chi^2$ test and Fisher's exact test for qualitative variables and the Mann-Whitney *U* test for quantitative variables. The survival rates were estimated using the Kaplan-Meier method and group comparisons using the log-rank test. All reported *P* values were 2-sided. For all statistical tests, differences were considered significant at the 5% level. Statistical analyses were performed using the STATA, version 13.0, software.

## Results

### *Patient Characteristics and Radiologic Findings*

From January 2000 to December 2012, 93 patients with pathologically confirmed SC were included. The patients were mainly male, with a gender ratio of 3.4 (74%). The mean age at diagnosis was 63 years (range, 40-85). Most patients were present or previous smokers (84% of patients), and the mean number of pack-years was 40 (range, 2-110 pack-years). Of the 93 patients, 85% presented with symptoms, which revealed the disease. At diagnosis, the WHO performance status was 0 to 1 for most patients (68%). The most frequent symptoms were fatigue (45%), cough (33%), weight loss (32%), thoracic pain (32%), and dyspnea (31%); 1 patient in 5 had presented with hemoptysis (21%). The clinical characteristics are summarized in Table 1.

Chest CT was performed in all patients. The mean tumor size was large, approximately 60 mm (range, 10-210 mm). Most tumors presented as a unique mass or nodule (86%) and were located in the peripheral field of the lung (56%). The upper lobes were most commonly involved (60%). A heterogeneous pattern of a cavity inside the tumor was observed in 20% of the cases. Chest wall invasion was noted in 15 (18%) and pleural effusion in 25% of the cases. Twenty patients (22%) presented with clinical stage T4 disease (mediastinal invasion or metastases in another lobe of the ipsilateral lung). Clinical lymph node invasion was observed in 48% of the cases. Of the 93 patients, 17 (18%) had stage I disease, 11 (12%) had stage II disease, 24 (26%) had stage III disease, and 40 (43%) had stage IV disease.